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|---|---|
| CELSA, BENNETT M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | 13 |

DATE MAILED: 09/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

file copy

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/866,536 | Gluckman et al. |
| **Examiner** | **Art Unit** |
| Bennett Celsa | 1639 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *Jul 8, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above, claim(s) *8* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Response to Amendment*

Applicant's amendment dated 7/8/03 in paper no. 12 is acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Status of the Claims*

Claims 1-8 are currently pending.

Claims 1-7 are under consideration to the extent that they read on the elected invention.

Claim 8 is withdrawn from consideration as being directed to a nonelected invention..

### *Election/Restriction*

2. Applicant's election without traverse of GPE in Paper No. 10 (mailed 3/13/03) which reads on claims 1-7 is acknowledged.

3. Claim 8 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

4. This application contains claim 8 which is drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

***Withdrawn Objection (s) and/or Rejection (s)***

Applicant's claim amendment has overcome the indefinite rejection of the phrase "the functional symptoms of Parkinson's disease" for lack of antecedent basis.

Applicant's argument (e.g. GPE refers to Glu-Pro-Glu) has overcome the indefinite rejection of the metes and bounds of the term GPE.

Applicant's amendment (deleting analog or mimetic thereof) has overcome the indefinite rejection of these claims presented in the prior office action.

***Claim Rejections - 35 USC § 112***

5. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

B. In claim 1(and claims dependent thereon), use of the term "prophylaxis" is confusing in the presently claimed context regarding "a patient suffering from the functional symptoms of Parkinson's disease"; to the extent that "prophylaxis" is synonymous with prevention , which implies a host who is disease or symptom free. To the extent "prophylaxis" does not encompass prevention it is confusing as to how this term distinguishes from "treatment" as already claimed.

C. In claim 1 (and claims dependent thereon) use of the term "the functional symptoms of Parkinson's disease" is confusing as to the metes and bounds of this term and how "the functional symptoms" differ from "non-functional symptoms" of the same disease state.

E. In claim 1 (and claims dependent thereon), the metes and bounds of the term "prodrug" (of GPE) is confusing since the specification fails to provide a single definition of the term"prodrug" or even describe a single compound which is exemplary thereof.

F. Method claims 1-2,4-7 are incomplete since no method step is recited.

***Discussion***

Applicant's amendment and arguments directed to the above indefinite rejection were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the indefinite rejection in item E. above was modified in response to applicant's amendment.

Regarding item B. above, applicant argues that the term "prophylaxis" is well known to refer to preventing symptoms, which are in remission, from recurring in a Parkinson's patient.

Applicant's argument was considered but deemed nonpersuasive for the following reasons.

Applicant's definition of "prophylaxis" is within the scope of the term "treatment". Accordingly, either the term "prophylaxis" is redundant and should be deleted, or prophylaxic may be incorporated to encompass preventing the Parkinsonian symptoms in patients who don't have Parkinson's disease. Since, it is unclear as to what interpretation is encompassed, the claim fails to apprise one of ordinary skill in the art what would infringe or not infringe, thus rendering the claim indefinite.

Applicant's arguments directed to item C above (e.g. "the functional symptoms of Parkinson's disease") was considered but deemed nonpersuasive for the following reasons.

Applicant argues that a definition of "a functional symptom of Parkinson's Disease" is described on page 4 of the specification; thus rendering this phrase definite.

The Examiner respectfully disagrees. Initially, it is noted that Applicant's argument is not commensurate to the presently claimed invention which is not so limited. Additionally, the specification on page 4 refers to Parkinson's disease as " ... a chronic and progressive motor system disorder and is distinguished by a tremor at rest, muscular rigidity, a slowness of movement initiation, and movement execution and a mask-like appearance to the face". As such the specification, contrary to applicant's assertion, does not specifically provide a definition of the term "functional symptom of Parkinson's Disease"; nor does the specification indicate that "tremor at rest, muscular rigidity, a slowness of movement initiation, and movement execution and a mask-like appearance to the face" represent the only species of functional symptoms of Parkinson's Diseases within the scope of possible Parkinson functional symptoms. Nor are the claims specifically limited to these manifestations of Parkinsons as being the only functional symptoms. In this regard, the specification (e.g. pages 1-3 ) and applicant's own examples describe other manifestations of centrally system neurological disorder damage (e.g. Parkinsons) which include hypoxia, hemorrhage, infarction, ischemia, loss of dopaminergic neurons etc. which would be within the scope of functional Parkinson disease symptoms.

Turning to item E. above applicant argues that deleting "analog of GPE" and "mimetic of GPE" has overcome the indefinite rejection.

Applicant's argument and amendment were considered but deemed nonpersuasive since the amendment did not delete prodrugs of GPE nor did applicant's arguments address this aspect of the rejection.

Turning to item F above, applicant argues that the term "increasing" is a method step well known in the art and Applicant requests that the Examiner provide an Affidavidit/Declaration including evidence that the term "increasing" is not a method step.

Applicant's arguments were considered but deemed nonpersuasive for the following reasons.

Applicant's argument fails to address the crux of the indefinite rejection above which asserts that the presently claimed method is incomplete. In accordance with case law (e.g. *In re Mayhew)* and the MPEP (e.g. MPEP 2172.01) a claim which omits essential matter, including a method step" described by the specification to be necessary to practice the claimed invention, renders the claim indefinite. Applicant's claim requires "increasing the effective amount of GPE within the CNS of said patient", wherein the determination of effective amounts of GPE (e.g. proper dosage) can only be determined upon administration (E.g. see specification pagees 4-5) . Accordingly, the claim fails to recite the requisite means of increasing the *effective* amount of GPE and as such is an incomplete method claim. It is the burden of applicant (not the Examiner) to render the claimed method definite so as to apprise one of ordinary skill in the art what will or will not infringe the claimed invention.. It is noted that amending to insert the claim 3 limitation into claim 1, in light of the specificatioin teaching, will serve to overcome this rejection.

Accordingly, the above indefinite rejections are hereby maintained.

6. Claims 1-3 and 5-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (LACK OF WRITTEN DESCRIPTION).

Claims 1-3 and 5-7 describe "increasing the effective amount of GPE within the CNS of said patient" e.g. by the use of Gly-Pro-Glu **and prodrugs"** for treatment or prophylaxis of a patient suffering from a functional symptom of Park*insons disease* . However, the metes and bounds of GPE increasing compounds (e.g. prodrugs) is unclear. The specification fails to provide a single definition of the term "prodrug" of GPE; nor does it describe a single compound which is exemplary thereof..

Thus, the claimed invention encompasses an untold number of different compounds of different structure (e.g. potential deletion/substitution/addition or other alteration of a starting structure) which need not share any decipherable common core structure relative to the reference compound (Glu-Pro-Gly).

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it

from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to a generic of compounds; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the compound or generic(s). For example, in a recent court case in line with *Eli Lilly, Judge Lourie writing for the CAFC* made the following observation:

> "A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) having the function of lessening inflammation of tissues, fails to distinguish any steroid from others having the same activity or function. Similarly, the expression "an antibiotic penicillin" fails to distinguish a particular penicillin molecule from others possessing the same activity. "

See: J. Lourie decision in *Enzo Biochem, Inc. v. Gen-Probe Inc. et al.* No. 01-1230 (CAFC: Decided April 2, 2002) (citation forthcoming).

In this regard, applicant is referred to the seminal case of *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and the "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001).

It is noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.*

As pointed out above, the specification discloses only limited examples that are neither representative of the claimed GPE increasing "prodrug" compounds of GPE.

***Discussion***

Applicant's amendment and arguments directed to the above written description rejection were considered but deemed persuasive with regard to GPE increasing analogs or mimetics but unpersuasive with regard to other GPE increasing prodrug compounds. The above rejection was revised in response to applicant's amendment.

Applicant argues that it is known in the art that certain peptides can be cleaved by peptidases (or proteases) to result in formation of shorter peptides as exemplified by IGF-1 cleavage to des(1-3 IGF-1) as described on page 3 of the specification. Applicant therefore asserts that the term "prodrug" of GPE includes peptides, including but not limited to IGF-1, that

upon cleavage result in formation of GPE. Thus, applicant argues that contrary to the Examiner's office action, Applicant's have provided a description of a "prodrug" of GPE, namely IGF-1.

Applicant's argument was considered but deemed nonpersuasive for the following reasons. First, the specification fails to provide a definition or description which delineates sufficient identifying core structure for one of skill in the art to distinguish the structure which necessarily distinguishes a GPE prodrug from a compound which is not a GPE prodrug. In this respect, a single species of GPE prodrug, IGF-1 is simply not representative of an open-ended generic of possible compounds of variable structure which may or may not resemble GPE but yet function as a prodrug e.g. "increase the effective amount of GPE within the CNS of said patient". For example any means of increasing the effective amount of CNS GPE could conceivably constitute a prodrug which would encompass peptides of variant structure as well as non-peptides. For example the following may be classifiable as prodrugs:

a. Any compound which degrades in vivo to GPE or is converted by amino acid deletion/substitution/addition or otherwise into GPE;

b. gene therapy (e.g. the intracellular incorporation of genetic material) which serves to result in the intracellular recombinant production of GPE within the CNS of a patient;

c. any compound which inhibits CNS degradation of GPE;

d. any compound which upregulates the production of GPE.

Accordingly, applicant's claims directed to "increasing the effective amount of GPE within the CNS" (e.g. use of a prodrug) and specification description of a single species of prodrug, without

more, fails to distinguish any compound which increases the effective amount of GPE (e.g. a prodrug) from others having the same activity or function.

Applicant argues that unlike Lilly, "in the instant case, all "prodrugs" of GPE contain the exact sequence, GPE" and "Applicant's further submits that GPE can be detected and measured using methods that are routine in the art.

These argument were considered but deemed nonpersuasive for the following reasons.

Applicant's first argument (e.g. all "prodrugs" of GPE contain the exact sequence, GPE) is not commensurate to the claimed invention which is not so limited, nor is it necessarily supported by the specification. Secondly, assuming arguendo applicant's assertion is true, there is no metes and bounds as to what additional chemical structure is present to distinguish GPE derivatives from others having the same activity or function. Applicant's next argument "that GPE can be detected and measured using methods that are routine in the art", even assuming arguendo that the specification and/or prior art provides such methods, nonetheless although applicable to enablement, does not serve to provide descriptive support.

Applicant further argues that the claims don't lack written descriptions since GPE is clearly defined (e.g. as Gly-Pro-Glu) and only one mechanism (e.g. "increasing the effective amount of GPE") is claimed (e.g. to define a prodrug).

This argument is not convincing for the reasons recited above e.g. there is no specification definition of GPE prodrug and thus it encompasses any compound (or device for that matter) which is capable of "increasing the effective amount of GPE within the CNS" of a patient, which

is a result (not a mechanism as asserted by applicant), which can occur via a number of different unrelated mechanisms. Additionally, the disclosure of one compound species of specific peptide structure which is asserted to be a prodrug is not representative of other compounds (or devices) which can achieve the claimed means of "increasing the effective amount of GPE within the CNS of said patient" via administration or otherwise (e.g.applicant's claims are not limited to the administration of a compound but encompass any means of increasing CNS GPE amounts as discussed above).

Applicant argues that the Written Description Guidelines do not have the force of law.

Although the Guidelines do not have the force of law, applicant cannot ignore numerous caselaw, both prior and subsequent to the Guidelines, which requires conformance with the written description requirement.

Applicant further argues that the presence of the term "prodrug of GPE" as an original claim entitles it to a "strong presumption that an adequate written description of the claimed invention is present when the application is filed".

However, this presumption is rebuttable, and has been rebutted in the above written description rejection.

Accordingly, the above written description rejection, as modified, is hereby maintained.

7. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a method of protecting dopaminergic neurons against death resulting from Parkinson's disease using a neuroprotective amount of Gly-Pro-Glu as described in the examples; the specification does not reasonably provide enablement for the scope of prodrugs of Gly-Pro-Glu to treat all "a functional symptom of Parkinsons disease" as presently claimed. The specification does not enable nor provide sufficient description, for any person skilled in the art to which it pertains; or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

1. The breadth of the claims.

2. The nature of the invention

3. The state of the prior art;

4. The level of one of ordinary skill

5. The level of predictability in the art;

6. The amount of direction provided by the inventor;

7. The presence or absence of working examples;

8. The quantity of experimentation necessary needed to make or use the invention based on the disclosure;

See :*In re Wands* USPQ 2d 1400 (CAFC 1988):

*(1-2) The breadth of the claims and the nature of the invention*:

Claims 1-7 describe "increasing the effective amount of GPE within the CNS of said patient" e.g. by the use of Gly-Pro-Glu **and prodrugs"** for treatment or prophylaxis of a patient suffering from a functional symptom of Parki*nsons disease* . However, the metes and bounds of GPE increasing compounds (e.g. prodrugs) is unclear. The specification fails to provide a single definition of the term "prodrug" of GPE; nor does it describe a single compound which is exemplary thereof..

Thus, the claimed invention encompasses an untold number of different compounds of different structure (e.g. potential deletion/substitution/addition or other alteration of a starting structure) which need not share any decipherable common core structure relative to the reference compound (Glu-Pro-Gly).

3 and 5) *The state of the prior art and the level of predictability in the art:*

In accordance with the present invention, the ability of a ligand (e.g. a hormone) to predictably bind a receptor is a prerequisite for obtaining "biological activity". However, ligand/receptor binding is stereospecific (e.g conformationally sensitive).(see Rudinger, Peptide Hormones (June 1976: J Parsons editor) pages 1-6; e.g. see page 4; and accordingly, the efficacy of binding of a ligand (e.g. cyclopentapeptide) to a receptor (e.g. enzyme/hormone etc.) to achieve physiological action is determined by the conformation of the given ligand. Thus the different aspects of biological activity cannot be predicted *a priori* but must be determined on a

case to case base through experimental study. The careful design of synthetic analogues and their evaluation in biological systems which permit separate analysis of the various phases of receptor (e.g hormone) action is the best way of obtaining such information. See Rudinger, Peptide Hormones, (June 1976) (J.A. Parsons, editor) 1,5-6.

Further, Applicants are reminded that claims drawn to pharmaceutical use (e.g. the making of biologically active peptides) generally require supporting data which is both commensurate in scope and extrapolatable to human efficacy in view of the unpredictability in biological responses of pharmaceutical treatments. For the efficacy of a drug treatment in vivo faces unfavorable obstacles not present in vitro. For example, drug delivery to the targeted area must survive the acidic environment of the stomach if administered orally. Additionally, the drug if indeed immunogenic as many drugs are, must survive an antibody response which may act to deactivate the drug before it achieves its situs or desired response. For the delivery of the drugs to and/or across necessary cell surfaces in amounts needed to be efficacious, but not lethal to the organism, necessitates sensitive testing in order to adequately determine the proper human dosage.

(4) *The level of one of ordinary skill in the art:*

The level of skill would be high, most likely at the Ph.D. level.

(6-7) *The amount of direction provided by the inventor and the existence of working examples.*

The specification only provides support (e.g. examples) for using Gly-Pro-Glu for its neuroprotective properties relating to protecting dopaminergic neurons from cell death e.g. as resulting from Parkinson's disease.

*(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure:*

*Thus,* the specification discloses only limited examples that are neither representative of the claimed genus of compounds; nor does the disclosure of a handful of specific peptides comprising core peptide motifs and the in vitro receptor binding of related peptides represent a substantial portion of the claimed genus Accordingly, the undue breadth of possible "biologically active" (e.g. increase effective GPE CNS amounts in patients) compounds i.e. GPE prodrugs; the unpredictable effects on bioactivity of subtle changes to the chemical structure and the stereospecificity necessary for receptor/ligand binding, the lack of guidance presented in the specification, the lack of representative examples for both making and use, necessitate the illustration of further examples demonstrating the making and use of a representative sample of peptide (or non-peptide) compounds along with a showing which is reasonably predictive and commensurate of *in vivo* utility in order to provide the requisite enablement for the presently claimed invention as broadly claimed.

***Discussion***

Applicant's amendment and arguments directed to the above enablement rejection were considered but deemed persuasive with regard to GPE increasing analogs or mimetics but not

persuasive with regard to other GPE increasing prodrug compounds. The above rejection was revised in response to applicant's amendment.

Applicant argues that the Examples in the specification provide direct evidence, *in vivo*, of the efficacy of the claimed invention.

This argument is not persausive since applicant's arguments are not commensurate to the presently claimed invention which is not limited to administering GPE to treat or prophylax functional symptoms of Parkinson's disease within the scope of the presently claimed invention.

Applicant further argues that "discovering a positive correlation between increasing GPE and improvement in any functional symptom" is sufficient to teach one of ordinary skill in the art how to make and use the invention for the scope of the claims.

This argument was considered but deemed nonpersuasive since it is not commensurate to the presently claimed invention which is not limited to administering GPE nor is administeringGPE (or IGF-1) as in the examples representative of the scope of the presently claimed invetion which encompasses "increasing the effective amount of GPE within the CNS" by means other than administration of GPE (or IGF-I) as discussed above. For example, since there is no specification definition of GPE prodrug and thus it encompasses any compound (or device for that matter) which is capable of "increasing the effective amount of GPE within the CNS of said patient. Additionally, the disclosure of one compound species of specific peptide structure as a prodrug is not representative of other compounds (or devices) which can achieve the claimed means of "increasing the effective amount of GPE within the CNS of said patient" via

administration or otherwise (e.g.applicant's claims are not limited to the administration of a compound but encompass any means of increasing CNS GPE amounts as discussed above. In light of the unpredictability in the art, where conservative amino acid substitutions can lead to inactivity, as discussed in the above rejection and the scope of compounds which may serve to increase GPE CNS amounts the presently claimed invention is clearly not enabled for both making and using for the scope of the claims.

Applicant argues that "Issues relating to drug delivery and pharmacokinetic properties are not relevant to in vivo demonstration of the utility of 'increasing the effective amount of GPE' to treat a functional symptom of Parkinson's disease"; and "The fact that the animals survived in vivo treatment indicates that the drugs were not lethal .... consideration of toxicity, if present, is not relevant to patentability of the claims under the instant circumstances.

Applicant's arguments were considered but deemed nonpersuasive for the following reasons. Initially, it is noted applicant is misguided insofar that the above rejection does not address toxicity issues which is clearly within the purview of the FDA. However, the rejection does address efficacy issues which is relevant, in contradistinction to applicant's argument, since it addresses issues related to unpredictability and the necessity of enabling efficacious drugs e.g. by teaching the making and use of representative drugs and their corresponding efficacious administration and dosage regimens.

Accordingly, the above enablement rejection is hereby maintained.

***Claim Rejections - 35 USC § 102 and 103***

8. Claims 1-3 and 5-7 are rejected under 35 U.S.C. 102(a,b) as being anticipated by Gluckman, WO 93/02695 (2/93).

Gluckman teaches administering IGF-1 (an analog/mimetic/prodrug of GPE as taught in the present specification pages 9-10) and analogues thereof to "treat" CNS injuries which are as "a consequence of Parkinson's disease" by "direct administration (e.g. shunt). The disclosure of "Functional symptoms" (e.g. hypoxia/ischemia /trauma /demylenation" of Gluckman are within the scope of "functional symptoms of Parkinsons disease" as presently (and broadly) claimed. See e.g. Gluckman Abstract; claims etc..

***Discussion***

Applicant's arguments directed to the above anticipation rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that the above reference fails to teach "A method for treating a functional symptom of Parkinson's disease", wherein "functional symptoms " are as newly defined by applicant.

However, applicant's arguments are not persuasive since applicant's argument is not commensurate in scope to the presently claimed invention which is not limited to any specific species of a "functional symptom". The Examiner maintains that the reference disclosure of "Functional symptoms" (e.g. hypoxia/ischemia /trauma /demylenation") is within the scope of applicant's invention as indicated by applicant's own specification (e.g pages 1-3) and examples

which include the recitation of hypoxia/ischemia/trauma/demylenation as being affiliated with neurological damage as present in Parkinson patients. It is also noted that the Gluckman reference teaches both "treatment" and "prevention" (e.g. see Gluckman pages 3-4) of functional symptoms related to Parkinson's disease patients (e.g see Gluckman claims 1 and 7).

Accordingly, the above rejection is hereby maintained.

9. Claims 1-7 are rejected under 35 U.S.C. 102(a,e) as being anticipated by Gluckman et al., US Pat. No. 6,187,906 (2/2001: filed 6/99 or earlier).

Gluckman et al. disclose and claim a method of protecting (e.g. treatment/prophylaxis) dopaminergic neurons (against cell death e.g. functional symptoms of Parkinson's i.e. involving dopaminergic neurons) by administering (e.g. directly to the brain): gly-pro-glu (GPE) . See abstract; examples; patent claims.

***Discussion***

Applicant's arguments directed to the above anticipation rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that the above reference fails to teach "A method for treating a functional symptom of Parkinson's disease", wherein "functional symptoms " are as newly defined by applicant.

However, applicant's arguments are not persuasive since applicant's argument is not commensurate in scope to the presently claimed invention which is not limited to any specific species of a "functional symptom". The Examiner maintains that the reference disclosure of "Functional symptoms" (e.g. cell death) is within the scope of applicant's invention as indicated by applicant's own specification (e.g pages 1, line 29) and examples (e.g. example 5).

Accordingly, the above rejection is hereby maintained.

10. Claims 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noble et al. US Pat. No. 5,762,922 (6/98).

Noble et al. teach the treatment of diseases or conditions characterized by an insufficiency of a particular cell type (E.g. brain) by administration (e.g. including direct administration: e.g. see col. 7-8) of growth factors (including IGF-1) wherein the disease state is Parkinsons. E.g. see patent claim 1; patent claim 4 directed to Parkinson's. The selection of growth factors (or IGF-1) (e.g. which qualify as analogues/mimics/prodrugs of GPE) which treat Parkinsons would have been prima facie obvious to one of ordinary skill in the art since the selection of such growth factors and parkinson's represent preferred embodiments as evidenced by the patent claims.

***Discussion***

Applicant's arguments directed to the above obviousness rejection were considered but deemed nonpersuasive for the following reasons.

Applicant first argues that the above reference fails to teach "A method for treating a functional symptom of Parkinson's disease", wherein "functional symptoms " are as newly defined by applicant.

However, applicant's arguments are not persuasive since applicant's argument is not commensurate in scope to the presently claimed invention which is not limited to any specific species of a "functional symptom" and treating/preventing e.g. "cell death" (e.g."insufficiency of a particular cell type" as claimed in the patent: see col. 3) resulting from Parkinson's disease is within the scope of applicant's invention as indicated by applicant's own specification (e.g pages 1, line 29) and examples (e.g. example 5)..

Applicant next argues that Noble et al. fails to provide the use of GPE . This argument was found persuasive with respect to present claim 4 which is so limited; and accordingly, the above rejection was modified to exclude claim 4. With respect to the other claims, the reference provides explicit motivation (e.g. in patent claims) to utilize IGF-1 to treat/prevent a functional symptom of Parkinsons disease; the use thereof (e.g. IGF-1) which is clearly within the scope of the presently claimed invention.

Accordingly, the above rejecition, as modified, is hereby maintained.

***Double Patenting***

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No.6,187,906 (2/2001) . Although the conflicting claims are not identical, they are not patentably distinct from each other because Gluckman et al. claim a method of protecting (e.g. treatment/prophylaxis) dopaminergic neurons (against cell death e.g. functional symptoms of Parkinson's i.e. involving dopaminergic neurons) by administering (e.g. directly to the brain): gly-pro-glu (GPE) .

***Discussion***

Applicant's arguments directed to the above double patenting rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that the above patent claims fails to teach "A method for treating a functional symptom of Parkinson's disease", wherein "functional symptoms " are as newly defined by applicant.

However, applicant's arguments are not persuasive since applicant's argument is not commensurate in scope to the presently claimed invention which is not limited to any specific species of a "functional symptom". The Examiner maintains that the reference disclosure of "Functional symptoms" (e.g. cell death) is within the scope of applicant's invention as indicated by applicant's own specification (e.g pages 1, line 29) and examples (e.g. example 5).

Accordingly, the above rejection is hereby maintained.

***New Objection(s) and/or Rejection (s)***

***Claim Objections***

13. Claim 2, line 2 is objected to because of the following informalities: "symprom" .

*Conclusion*

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

**General information regarding further correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang (art unit 1639), can be reached at (703)306-3217.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1639)

September 16, 2003

BENNETT CELSA
PRIMARY EXAMINER